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The effect of polycystic ovary syndrome on intracytoplasmic sperm injection results in patients with endometriosis

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ABSTRACT

Aim: In this study, the fertility rate of women with polycystic ovary syndrome (PCOS) and endometriosis was compared with the control group, which included women with normoresponder (NR) endometriosis.

Material and Method: This is a retrospective study with control in infertile women aged 25-40, suffering from PCOS and endometriosis, referred to the infertility clinic of Medistate Hospital between September 2018- December 2020. The pregnancy outcomes of age-matched participants were compared.

Results: Results did not show a statistically significant association between case and control regarding age and body mass index (BMI) ($p>0.05$). There was a statistically significant difference between groups regarding anti-mullerian hormone (AMH) ($p<0.05$). Also, results did not find a statistically significant association between case and NR endometriosis regarding positive pregnancy outcomes ($p>0.05$).

Conclusion: Women with PCOS and endometriosis did not show a significant difference in terms of pregnancy outcome compared to women with NR women with endometriosis.

Keywords: Polycystic ovary syndrome, intracytoplasmic sperm injection, endometriosis

INTRODUCTION

In endometriosis, the endometrial tissue of the uterus extends out to the pelvic space,peritoneum and on to the organs like ovaries, intestines and the bladder. The disease spectrum is vast and ranges from large endometrioma cysts to small lesions on the pelvic organs, creating significant adhesions in the uterus, bladder and intestine and disrupting the anatomy of the pelvis (1-3). The disease treatment is still associated with many problems. Next to clinical examination and medical technologies such as imaging techniques and biomarkers, laparoscopy was the standard diagnostic method. The disease has different severities and the probability of the disease returning after drug treatments and surgery is high (4).

Some studies showed that the pregnancy rate is reduced in endometriosis patients because of abnormal folliculogenesis, decreased ovarian follicular reserve and reduced oocyte fertilization ability (5). Also, other studies showed that the in vitro fertilization (IVF) success rate in endometriosis patients is lower than in other patients (6). Also, the oocyte numbers, good-quality embryos, fertilized oocytes, and fertility success rate in endometriosis patients are low (7). In addition, an inverse relationship between the severity and degree of this disease and the monthly fecundity rate (MFR) has been reported (8). Some studies show a decrease in MFR and pregnancy and a decrease in embryo implantation after IVF in women with endometriosis (9). Endometriosis surgery and treatment have potential risks, benefits, and long-term effects on the quality of life that patients undergoing surgery should be informed about it (10).

On the other hand, polycystic ovary syndrome (PCOS) is a prevalent endocrine disorder that affects 5-10% of women of reproductive age (5). The complex pathophysiology of PCOS involves chronic anovulation, high androgen levels, insufficient secretion of gonadotropins, and abnormal ovaries morphology (7). The clinical disorders of PCOS are infertility, hirsutism, irregular menstrual cycles or amenorrhea, acne, and hair loss (7). In PCOS patients, insulin resistance and obesity

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are the pathophysiology principles. As a result, the insulin increase in these patients stimulates the ovarian androgen production (11).

There are controversial opinions regarding the cause and treatment of infertile women who suffer from PCOS. Retrospective and prospective studies reported PCOS as a risk factor for increased pregnancy complications (5). Various studies reported an increased risk of premature birth, preeclampsia, gestational diabetes and hypertension, an increased risk of admission to the intensive care unit, and a mortality rate for newborns in pregnant patients (8,12). Some reports show an increase in the spontaneous abortion rate in PCOS patients (6). Complications of the first trimester of pregnancy in PCOS patients include congenital abnormalities of the fetus and miscarriage (8).

Due to the prevalence of PCOS and insufficient information on the pregnancy outcome of mothers with a history of PCOS, this study compared pregnancy outcomes of normoresponder endometriosis and PCOS/endometriosis patients underwent intracytoplasmic sperm injection (ICSI) to investigate the effect of PCOS in patients with endometriosis.

MATERIAL AND METHOD

This study was carried out with the permission of Beykoz University Ethics Committee (Date: 18.02.2021, Decision No: 1). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

This is a retrospective study with control in infertile women aged 25-40, suffering from PCOS and endometriosis, referred to the infertility clinic of Medistate Hospital between September 2018- December 2020. In this study, the total number of participants was 105 in two groups (54 with PCOS and endometriosis in the study group and 51 with normoresponder (NR) endometriosis in the control group). The pregnancy outcomes of age-matched participants were compared retrospectively.

Diagnosis of endometriosis was made by ultrasound and laparoscopic. Cases with male factors, chronic disease, and recurrent implantation failure were excluded from the study. Patients aged 25-40, with the first trial of ICSI with no other additional infertility factor are included.

Statistical Analysis

The Kolmogorov-Smirnov test was performed to check the normality. Mean and standard deviations (SD) were measured to check each continuous variable, including age, body mass index (BMI), age of menarche, anti-mullerian hormone (AMH), follicle-stimulating hormone (FSH), luteinizing hormone (LH), estradiol (E2), free testosterone, dehydroepiandrosterone sulfate (DHEA-SO4), fasting blood sugar (FBS), Hemoglobin A1C (HBA1C), prolactin (PRL), metaphase 2 (MII), number of embryos transferred (TEENS), number of embryos total oocyte, number of cryopreserved embryos, implantation rate and gestational sac. In all variables except free testosterone, the Mann-Whitney U test was performed to examine the difference between the two groups. in free testosterone, due to its normality, Independent t-test was used. SPSS v22was used for statistical analyses. A value of $p < 0.05$ was accepted as statistically significant.

To calculate the sample size with the G-Power 3.1 program, two groups' total mean was measured based on the Mann-Whitney test with the power of 95%, effect size of 50%, and 0.05 type 1 error for at least 92 patients (13).

RESULTS

This study included one hundred five age-matched (31.42±3.37) and BMI-matched (25.45±1.44) women. **Table 1** shows descriptive statistics of study parameters.

Table 1. Descriptive statistics of study parameters in the infertile group of women

Study parameters	median (range)	mean ± SD
Age	32 (25-39)	31.42±3.37
BMI	25 (23-29)	25.45±1.44
Age of menarche	11 (10-14)	11.31±0.94
AMH	4 (1.1-12)	3.97±2.38
FSH	8 (6-9)	7.76±0.64
LH	8 (4-16)	8.88±2.36
E2	45 (31-54)	44.08±4.91
Free testosterone	0.96 (0.2-1.62)	0.95±0.33
DHEA-SO4	286 (159-412)	283.26±60.47
FBS	88 (73-98)	88.03±6.86
HBA1C	5.29 (4-5.9)	5.19±0.51
PRL	18 (5-29.3)	18.83±5.39
Total oocyte	9 (3-32)	11.69±6.11
MII	8 (3-27)	9.92±5.25
PN	7 (2-20)	8.35±4.49
TEES	1 (1-2)	1.48±0.502
Cryopreserved embryo(n)	2 (0-8)	2.2±1.50

SD, standard deviation.

Table 2 shows the comparison of case and control groups on the study parameters. As stated in **Table 2**, a Mann-Whitney test did not find a statistically significant association between case and control regarding age and BMI ($p>0.05$). There was a statistically significant difference between groups regarding AMH ($p<0.05$). There was not a statistically significant difference between case group and controls in regard to age of menarche ($p=0.731$), FSH ($p=0.744$), E2 ($p=0.990$), and TEENS ($p=0.929$). There was a statistically significant difference between the case group and controls regarding

LH, free testosterone, DHEA-SO4, FBS, HBA1C and PRL ($p<0.05$). There was a statistically significant difference between the case group and controls regarding cryopreserved embryo ($p<0.05$).

Table 2. Comparison of case and control groups

Study parameters	Case (PCOS and endometriosis) (n=54) M±SD	Control (Normoresponder endometriosis) (n=51) M±SD	p value
Age	31.33±3.2	31.53±3.57	0.958*
BMI	25.43±1.57	25.49±1.3	0.618*
Age of menarche	11.33±0.93	11.29±0.97	0.731*
AMH	5.98±1.61	1.84±0.3	<0.001*
FSH	7.74±0.68	7.78±0.61	0.744*
LH	10.74±1.51	6.92±1.25	<0.001*
E2	44.07±6.05	44.1±3.37	0.990*
Free testosterone	1.06±0.3	0.85±0.34	<0.001**
DHEA-SO4	295.46±62.03	270.35±56.56	0.033*
FBS	91.06±5.19	84.84±7.01	<0.001*
HBA1C	5.4±0.35	4.99±0.57	<0.001*
PRL	20.08±4.92	17.5±5.6	0.028*
Total oocyte	15.44±6.4	7.73±1.74	<0.001*
MII	13.04±5.6	6.63±1.59	<0.001*
PN	11.11±4.76	5.43±1.01	<0.001*
TEES	1.48±0.5	1.49±0.5	0.929*
Cryopreserved embryo	2.54±1.68	1.84±1.22	0.013*

M, Mean; N, number of subjects; BMI, body mass index; AMH, Anti-Müllerian hormone; FSH, follicle-stimulating hormone; LH, luteinizing hormone; E2, Estradiol; DHEA-SO4, dehydroepiandrosterone sulfate; FBS, Fasting Blood Sugar; HBA1C, Hemoglobin A1C; PRL, Prolactin; MII, Metaphase 2 Cell; TEENS, Number of embryos transferred; PN, Pronucleus Cell. *A Mann-Whitney test ** Independent t-test.

As stated in **Table 3**, a Chi-square test did not find a statistically significant association between case and NRr endometriosis regarding positive pregnancy outcome ($p>0.05$).

Table 3. The significant relationship between case and control groups and pregnancy results

Variable		pregnancy (-) (n=53) n (%)	pregnancy (+) (n=52) n (%)	p-value
PCOS	Yes	24 (45.3)	30 (57.7)	0.203*
	No	29 (54.7)	22 (42.3)	

*A Chi-square test. (+), positive; (-), negative

As stated in **Table 4**, the women with PCOS had a 26.66% abortion and 40.74% live births. The women with NR had an 18.8% abortion and 35.2% live births

Table 4. Abortion and live birth statistics in two groups

Pregnancy outcome variables	Patients with NR endometriosis (n=51) n(%)	Patients with PCOS and endometriosis (n=54) n(%)
Positive HCG	22 (43.15)	30 (55.55)
Abortion	4 (7.85)	8 (14.81)
Live Birth	18 (35.3)	22 (40.74)

Figure shows that the case group had higher abortion and live birth rates than the controls.

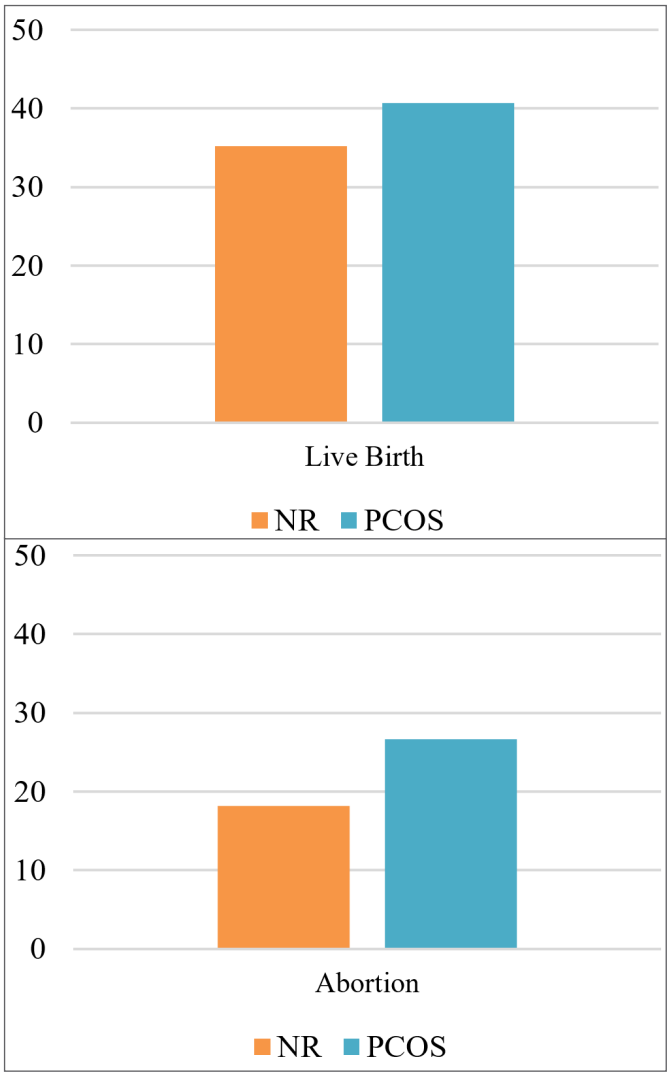

Figure. The effect of PCOS on the abortion and live birth rate

DISCUSSION

In this study, the fertility rate of women with PCOS and endometriosis was compared with the control group, which included women with NR endometriosis. For both groups, the ICSI-assisted treatment method was used for treatment. According to the results, women with PCOS and endometriosis did not show a significant difference in fertility compared to women with NR endometriosis group which is consistent with previous studies (14-16). In a similar study, Piltonen (17) showed that the embryo quality in endometriosis patients is not different from other referrals for ICSI. Examination of embryo quality in the present study also confirmed this finding. Therefore, it is suggested to control the inflammation caused by the disease before treating infertility by ICSI in endometriosis patients with medical or surgical treatments to increase the result of ICSI and its success rate (18,19).

Examination of fertility factors showed that although endometriosis caused the number of mature oocyte

obtained from these women to decrease after the treatment of the disease compared to the PCOS group, the pregnancy success rate from different aspects of pregnancy rate and live birth in the NR group of patients is not significantly different from the PCOS group. Some studies found that preterm delivery was more common in pregnant women with PCOS than in the control group (20,21). However, in others, which compared the results of pregnancy in women with PCOS based on age and weight with the control group, there was no statistically significant relationship between the two groups regarding the prevalence of premature birth (22).

In this study, the two PCOS and NR groups differ in the livebirth rate and abortion. In the study of Crespi (3), an increase in spontaneous abortion was reported in women with PCOS. Contrary to the above studies, the study by Alebić (1) showed that the rate of abortion in PCOS syndrome is probably not different from the control group. The difference could be because pregnant women with PCOS in previous studies were older than the control group, as age also plays a destructive role in increasing pregnancy complications (6). In the present study, only eight intrauterine deaths were reported in the PCOS group, which was not statistically significantly different from the NR group. In Zhai et al. (23), the rate of intrauterine death in both PCOS and NR groups was not statistically significant, which was consistent with the present study.

In the present study, the total oocyte number was higher in women with PCOS than in the NR group, which was statistically significant. In the study of Jiang et al. (9), which was conducted on pregnant women with PCOS, the total oocyte in the PCOS group was higher than in other disease groups, including NR, which was consistent with the present study. One of the limitations of this study was the low number of samples and lack of examination of the health factors of babies born from both groups. It is suggested, future studies should be conducted with a larger number of samples, in multiple medical centers, and with more variables related to the baby to draw more accurate conclusions.

CONCLUSION

The fertility rate of women with PCOS and endometriosis was compared with the control group, which included women with NR endometriosis. In conclusion, women with PCOS and endometriosis did not show a significant difference in fertility rate compared to women with NR.

ETHICAL DECLARATIONS

Ethics Committee Approval: This study was carried out with the permission of Beykoz University Ethics Committee (Date: 18.02.2021, Decision No: 1)

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper and that they have approved the final version.

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